

**REMARKS**

Claim 35 is amended. Support for claim 35 can be found, for example, at page 9, line 27 to page 10, line 29.

Claim 36 is amended to recite fewer compounds.

Claim 50 is amended to recite a method. Claim 58 is amended to clarify the claim language.

The rejection of claims 36 and 50 under 35 USC § 112, second paragraph is respectfully traversed. Claims 36 and 50 have been amended in accordance with the Examiner's suggestions.

The rejection of claims 35 and 41 – 58 under 35 USC § 103(a) over Upshall, Chem. Abstract 77:70055 is respectfully traversed. The Upshall abstract describes compounds having nicotinic activity, such as 2-(2-pyridinyl)-1,4,5,6-tetrahydropyrimidine. This compound from the Upshall abstract is structurally similar to compounds of the claimed invention. However, Applicants have provided evidence of unexpected results in the specification. In particular, the specification shows that the compounds of the claimed invention selectively activate  $\alpha 4\beta 2$  nicotinic acetylcholine receptors. The specification further shows that the compounds of the claimed invention have only a weak affinity for other receptor subtypes, such as  $\alpha 1\beta 1\gamma\delta$  receptors. (See, for example, the various Examples provided at pages 43 – 51 of the specification as filed.) This selective activation is valuable because the compounds of the claimed invention can selectively activate receptors in the central nervous system while reducing or

eliminating side effects in the peripheral nervous system. By contrast, the Upshall abstract alleges only general nicotinic activity. Based on the disclosure in the Upshall abstract, one of ordinary skill in the art would have no expectation that the compounds in the Upshall abstract could be used to selectively activate  $\alpha 4\beta 2$  nicotinic acetylcholine receptors.

Although the Upshall abstract discloses at least one structurally similar compound, Applicants' finding of selective activation of  $\alpha 4\beta 2$  nicotinic acetylcholine receptors by the compounds of the claimed invention is an unexpected result. As noted in the Office Action, a showing of unexpected results rebuts a prima facie case of obviousness over a structurally similar compound, and thus the compounds of the claimed invention are patentable over the disclosure in the Upshall abstract. Reconsideration and withdrawal of this rejection are respectfully requested.

The rejection of claims 35 and 41 under 35 USC 103(a) over Gauthier, et al., US Patent No. 4,379,926, is also respectfully traversed. The Office Action states that Gauthier et al. describes compounds that are structurally similar to the compounds of the claimed invention. The compounds of Gauthier et al. are described as having pharmaceutical activity as a diuretic in mammals. Gauthier et al. fails to note any nicotinic activity for its disclosed compounds.

As described above, Applicants have shown that the claimed compounds have the unexpected property of selective activation of  $\alpha 4\beta 2$  nicotinic acetylcholine receptors. Based on Gauthier et al.'s disclosure of compounds

having diuretic activity, one of ordinary skill in the art would have no expectation that the compounds of the claimed invention could be used to selectively activate  $\alpha 4\beta 2$  nicotinic acetylcholine receptors. This showing of unexpected results rebuts the prima facie case of obviousness, and thus the compounds of the claimed invention are patentable over the disclosure of Gauthier et al. Reconsideration and withdrawal of this rejection are respectfully requested.

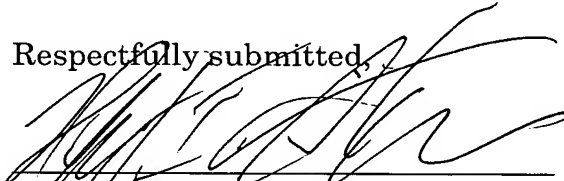
In view of the foregoing amendments and remarks, the application is respectfully submitted to be in condition for allowance, and prompt, favorable action thereon is earnestly solicited.

If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket #100598/50521).

March 16, 2004

Respectfully submitted,



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